Dear Healthcare Provider:

Please find enclosed information regarding Diphtheria antitoxin (DAT), an investigational product being provided by the Centers for Disease Control and Prevention (CDC), for treatment of suspected diphtheria in the U.S. given the lack of Food and Drug Administration (FDA)-approved drugs for treatment of diphtheria. CDC holds an expanded access (i.e., non-research) Investigational New Drug application (BB-IND 11184) filed with and authorized by FDA that allows for CDC to provide DAT to clinicians for compassionate use in patients with diphtheria. As DAT use is subject to FDA regulations (21 CFR parts 50, 56, and 312), please be advised that in requesting, obtaining, and administering investigational DAT, the treating clinician is serving as a site investigator for your patient's DAT treatment under the IND. Therefore, CDC respectfully requests that clinicians adhere to the enclosed DAT IND protocol (CDC IRB protocol #4167), including return of completed case report forms, to help ensure complying with the IND requirements and CDC's ability to continue to make DAT available under BB-IND 11184.

Central IRB Review of CDC IRB Protocol #4167: CDC's Institutional Review Board (IRB) serves as a central IRB for continuing review and approval of Protocol #4167 to facilitate timely, nationwide access to DAT for treatment of patients with suspected diphtheria. Please see **Appendix 7 of the protocol** regarding the option to use CDC's IRB approval of protocol #4167 in place of local IRB review.

Expiry extended use of DAT: The current lot of DAT (manufactured by Instituto Butantan in Brazil) provided under the IND has passed the manufacturer's original labeled expiration date (lot #200257 with original expiry of October 2022). Based on the totality of available information including prior experience with expiry-extended use of DAT, use of lot #200257 beyond its original labeled expiration date is allowed given the prolonged global shortage of DAT while newer product source is being actively pursued. CDC will provide updates and notify you of any changes that could affect the dose or effectiveness of the product.

Responsibilities, including delegated responsibilities, of the Treating Clinician:

- Upon or post receipt, if DAT is not used for the patient for whom it was requested, please return DAT to: CDC Drug Service H23-6; 1600 Clifton Road; Atlanta, GA 30329-4027 Telephone: 404-639-3670

  If you wish to use DAT in another patient, please notify the CDC Diphtheria Duty Officer Immediately by contacting CDC Emergency Operations Center at 404-788-7100.

- The case report forms (CRFs) are an **integral and required part of the IND to monitor adverse events and patient outcomes to the extent possible.** Please complete and return the following forms within 14 days of DAT administration to CDC Drug Service by fax (404-639-3717) or email (drugservice@cdc.gov):

  - **Appendix 1 (required):** Informed consent for administration of DAT must be obtained prior to treatment. A copy of this form should also be given to the patient and a copy should be maintained in your patient's medical records.
  - **Appendices 2–6 (required)**: DAT Treatment and Adverse Effects; CDC Diphtheria Worksheet; Information for Close Contacts; signed FDA 1572 (Statement of Investigator) and CV; Investigational Product Accountability and Disposition Form.
  - **Appendices 8a, 8b, 8c (as applicable):** Informed consent/parental permission/assent form(s) for additional blood draws.

CRFs are considered "past due" 30 days after DAT has been administered. If serious adverse events occur, you must notify CDC within 24 hours of occurrence or as soon as possible by contacting the CDC Diphtheria Duty Officer who was consulted at the time of DAT release. If this individual cannot be reached, the CDC Emergency Operations Center should be contacted at 770-488-7100 to reach the CDC Diphtheria Duty Officer on-call.